NON-FINAL ACTION

Applicant's amendment of 4-27-10 has been fully considered. Applicant's argument has overcome the previous 103 rejection based on **Moore et. al.** (US'891) in view of **Lohmann et. al.** (US'458), and thus, said rejection is now withdrawn. However, the amended claim 31 has not overcome the previous rejection of 112/1st paragraph. Thus, said 112/1st rejection is maintained herein. Also, other issues of 112/2nd are noticed which promp new ground of rejection.

Claims 30, 33 and 34 have been cancelled.

Claims 1-29, 31 and 32 are pending.

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

1. Claims 1-29 and 31 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being **enabling** for using compounds/compositions of formula I in **treating breast cancer, lung cancer, nasopharyngeal (head and neck) cancer, colorectal adenocarcinoma and kidney cancer** as per cell lines tested, does not reasonably provide enablement for other cancers such as: leukaemia, multiple myeloma, lymphoma, bile duct, bone, bladder, brain/CNS, endometrial, gastric, hepatic, neuronal, oesophageal, ovarian, pancreatic,

prostate, renal, skin, testicular, thyroid, uterine, and vulval. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The rejection is maintained for the reasons stated previously, and for the following:

a. The guidance provided is simply not in commensurate with the scope of cancers recited for the cell lines and compounds tested. For example, page 86, the bioassay for EGFR proliferation assay was done on KB cell (or human **naso-pharangeal** carcinoma). Another assay on page 87 is H16N-2 cell proliferation which used cells isolated from **human mammary tissue**. The *in-vitro* xenograft assay was on LoVo tumour (or colorectal adenocarcinoma). The last described assay is hERG-encoded Potassium Channel Inhibition Assay which used HEK (or **human embryonic kidney**). Because of different cell morphology, the data collected on the above cell lines cannot be extrapolated to other cancerous cells from another organs or tissues.

b. Out of about 109 species claimed herein, only two were actually tested for the inhibition of EGFR in KB cells. Thus, the result is not well represented for the range of compounds of the entire Markush group of formula I.

c. Regarding the treatment for leukaemia, multiple myeloma, lymphoma, **Gefitinib** (a commercial quinazoline EGFR inhibitor) possesses cytotoxic activity in acute myeloblastic leukaemia according to **Lindhagen et. al.** Besides, most chemotherapeutic agents would suppress bone marrow activity, and therefore, would have haematological

side effects such as: anemia, neutropenia, etc. which would be contraindicated in the treatment of leukaemia and related disorders.

For the reasons stated above, it is maintained that to select an effective compound from the large Markush group of formula I to treat a wide range of cancers, it would demand undue experimentation.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 9, 18, 26 and 32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

a. Claim 9 recites "R^a is positioned in the 2- and 3-positions of ring A..." However, R^a is not directly bonded to ring A, rather it is R^1. Thus, it is believed the position of R^a should have been that of R^1.

b. Claim 18 lacks antecedent basis because it depends on claim 1, but recites "(3-6C)cycloalkyl(1-3C)alkyl (2-6C)alkanoyl" for R^3 which is not recited in claim 1. It is believed a comma is missing that was meant to separate (2-6C)alkanoyl from the other moiety.

c. Claim 26 is inconsistent with the specification because it recites species that appear to be intermediates (e.g., p. 29, the 2nd and 7th compounds; p. 33, the 4th compound; p. 34, the first compound). Said compounds have *prolyl*, which is ***pyrrolidyl-C(=O)-O-***. However, their structures in the specification do not have the C(=O)-O- group.

d. Claim 32 recites the phrase "except that any functional group is protected if necessary" which renders the claim unclear because one does not know which functional group is intended. Would it be the funtional group directly bonded to the quinazoline or A ring? Or, would it be the fuctional group that is a substituent of R^1-R^6?

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TAMTHOM N. TRUONG whose telephone number is (571)272-0676. The examiner can normally be reached on Monday thru Friday (9:00-5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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/Tamthom N. Truong/
Examiner, Art Unit 1624

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7-26-10